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10/568,215

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Mary Lopez

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8128

37742

7590

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EXAMINER

SHEN, BIN

ART UNIT

PAPER NUMBER

1657

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/568,215	<b>Applicant(s)</b> LOPEZ, MARY	
	<b>Examiner</b> BIN SHEN	<b>Art Unit</b> 1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 24 June 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-3,5-17,19,21,22,24-27 and 30-34 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-3,5-17,19,21,22,24-27 and 30-34 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |                                                                                      |                                                                   |
|--------------------------------------------------------------------------------------|-------------------------------------------------------------------|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____                                                          | 6) <input type="checkbox"/> Other: _____                          |

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## **DETAILED ACTION**

### ***Status of the Claims***

Cancellation of claims 4 and 18 are entered. Claims 1-3, 5-17, 19, 21, 22, 24-28 and 30-34 are considered on the merits.

### **New rejections due to amendments of the claims:**

#### ***Claim Objections***

Claims 5, 6, 19, 21, 30, 31 are objected to because they dependent on cancelled claims. Appropriate correction is required.

#### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-12, 14-19, 21, 22, 24-25, 27-28, 30-32, 34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 15 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. Claims 1 and 15 are incomplete because even though the analyzing step is recited there is no method step on how the analyzing is accomplished. Further, the steps recited in claim 1 is a process for preparing sample for analyzing, there is no analyzing steps.

### **Maintenance of the rejection:**

#### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

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(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-3, 5-12, 14-17, 19, 21, 22, 24-25, 27-28, 30-32, 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Wagner et al. in view of each of Gygi et al. (PNAS 2000 97(17):9390-9395) and Kachman et al. (Anal. Chem. 2002 74:1779-1791).

Wagner teaches a process for analyzing proteins in a sample comprising dividing a sample into plurality of aliquots (page 810, right column, 5<sup>th</sup> and 6<sup>th</sup> full paragraph); applying to a first separation step to yield a plurality of partially resolved eluates; subjecting said plurality of partially resolved eluates to a second separation step; collecting at least one of said plurality of resolved fractions (page 811, left column, 1<sup>st</sup>-3<sup>rd</sup> full paragraph, **Claims 2 & 16**); analyzing the resolved fractions by mass spectrometry (page 813, left column, 1<sup>st</sup> full paragraph); wherein collection of the at least one of said plurality of resolved fractions occurs onto a MALDI target (page 813, left column, 1<sup>st</sup> full paragraph, **Claims 3, 5, 6, 17, 19, 31**); wherein the separation steps separate on a basis selected from the group consisting of: charge, molecular weight, and hydrophobicity and using chromatography resin, and the separation buffer varies monotonically between individual aliquots, and the separation steps comprises a separation matrix in linear (page 811, left column, 1<sup>st</sup>-3<sup>rd</sup> full paragraph, and page 812, Fig. 1, **Claims 8, 9, 22**) or two-dimensional array (page 811, right column, under 2D-HPLC system, **Claims 10, 11, 24, 25**).

Wagner does not teach that the mass spectrometry is performed on an orthogonal MALDI mass spectrometer, digesting a plurality of partially resolved eluates with a proteolytic enzyme to yield a plurality of digested eluates, labeling a sample with tagged or machine-readable labels, applying a plurality of aliquots in parallel to first separation step by a robot. However, Wagner suggests the automation of the process using robotic equipment (page 820, right column, 1<sup>st</sup> full paragraph, line 7. part of **Claim 32**).

Gygi teaches a method of protein analysis comprising tryptic digestion of samples before separated by chromatography (page 9393, right column, 1<sup>st</sup> full paragraph, line 8, **Claims 14 & 30**) in mass spectrometry for protein identification (abstract), and suggests to develop novel

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techniques that permit large-scale (automation) quantitative comparison of protein expression (page 9395, right column, end of Conclusions, part of **Claim 32**).

Kachman teaches a method of protein analysis by tagging protein in fraction in mass mapping method for interlysate comparison of protein expression (abstract, line 14, also see page 1786, left column, lines 16-18), and its potential to be automated (page 1791, right column, line 2, **Claims 32, 33, 34**).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Wagner by digesting and tagging protein samples in each fraction to analyze protein with orthogonal MALDI mass spectrometer for improved accuracy (**Claims 1, 7, 15, 21**) because Wagner teaches that multidimensional separation can be performed on digested protein (page 810, right column, 1<sup>st</sup> full paragraph) and Gygi teaches a digestion step in the mass spectrometer protein analysis, and simply repeat different separation steps with multiple samples is obvious to one of ordinary skill in the art to obtain predictable results. One would have been motivated to make the modification and automate the process using a robotic equipment because Wagner et al. specifically described the benefits of on-line array fractionation onto targets for MALDI-TOFMS (page 820, right column, 1st full paragraph), and would reasonably have expected success in view of Kachman's teaching of a protein tagging method for accurate mass analysis (page 1786, left column, lines 16-18) and its potential for automation.

A person of ordinary skill in the art, upon reading the references, would also have recognized the desirability to improve the method by performing the separation process multiple times either simultaneously as in parallel processing or sequentially for the obvious time saving by automation with predictable success because a person of ordinary skill has good reason to pursue the known options within his/her technical grasp.

Claims 1-3, 5-6, 8-11, 13, 26, 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Wagner et al. in view of Miliotis et al. (2000).

Wagner teaches what is above.

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Wagner does not teach that the separation steps occurs within a microplate with matrices maintaining well addresses in each of the two matrices, the collection (fractions/eluates affixing a machine-readable label.

Miliotis teach a process for analyzing proteins where the chromatographic separation is continuously transferred onto a plate as discrete spots (fractions/eluates) in a precise array pattern (abstract, lines 5-6, **Claims 12, 13, 26, 27**).

A person of ordinary skill in the art at the time the invention was made would have been motivated to develop an integrated protein identification platform using microplate to substitute for the MALDI target plate and collect fraction/eluates in a precise array patter because Miliotis teach the transferring of the separation fraction onto a MALDI target plate in an array (abstract; Fig 1).

Hence, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to affixing a machine-readable label to the fraction/eluates collection to simplify automation and increase the robustness of the system (see motivation for this improvement on page 109, end of the left column).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's arguments filed 6/24/2009 have been fully considered but they are not persuasive.

Applicant argues that Wagner fails to teach or suggest application of samples to a plurality of simultaneous different first separation steps to yield a plurality of uniquely different partially resolved eluates.

It is the examiner's position that the steps of claim 1 is a two step purification procedure with multiple columns and multiple samples (in parallel), thus it is obvious for a person of ordinary skill of art after reading Wagner's teaching to simply repeat the purification step with

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multiple columns to obtain plurality of purified factions, which does not change the result of the process (with predictable result), thus a person of ordinary skill in the art after reading the cited references for the purpose of saving time/automation (as taught by Kachman on page 1791, right column, line 2) would improve the method by performing the separating steps multiple times either in parallel or sequentially for the anticipated success as taught by Wagner. Furthermore, the last step of claim 1 recites “analyzing at least one of said plurality of resolved fractions”, and Wagner certainly analyzes at least one purified fraction.

Applicant argues that Gygi fails to teach large-scale (automation) quantitative comparison of protein expression; and Kachman fails to teach affixing a machine readable label.

It is the examiner's position that Gygi suggest “it is necessary to develop novel techniques that allow for...permitting large-scale quantitative comparison of protein expression” (page 9395, right column, Conclusion, lines 8-11) by using techniques other than 2DE-MS/MS, therefore Gygi provides motivation to explore different ways of achieving automation of the system with predictable results. Kachman teaches successful tagging of the protein in differential display (page 1786, Fig. 3) from Rotofor, and the different tag (displayed with different color) can be read as machine readable label because the machine (Rotofor) maps the differential display of protein expression from different cell lines.

### ***Conclusion***

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

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however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Certain papers related to this application may be submitted to Art Unit 1657 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone number for the Group is 571-273-8300. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Any inquiry concerning rejections or objections in this communication or earlier communications from the examiner should be directed to Bin Shen, whose telephone number is (571) 272-9040. The examiner can normally be reached on Monday through Friday, from about 9:00 AM to about 5:30 PM. A phone message left at this number will be responded to as soon as possible (i.e., shortly after the examiner returns to her office).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached at (571) 272-0925.

*B Shen*

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/Karen Cochrane Carlson/

Primary Examiner, Art Unit 1656